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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/699,679	10/30/2000	Evan C. Unger	UNGR-1598	8248

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EXAMINER

SHARAREH, SHAHNAM J

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 11/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/699,679

Applicant(s)

UNGER ET AL.

Examiner

Shahnam Sharareh

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 July 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3,4,6-17,22-35,61 and 63-67 is/are pending in the application.
- 4a) Of the above claim(s) 12 and 13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) 66 and 67 is/are allowed.
- 6) ☒ Claim(s) 3,4,6-11,14-17,22-35,61 and 63-65 is/are rejected.
- 7) ☒ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

JSD

DETAILED ACTION

1. Amendment filed on July 29, 2005 has been entered. Claims 3-4, 6-17, 22-35, 61, 63-67 are pending.

In Paper No. 22B, filed on April 10, 2003, Applicant made an election of for the claims categorized in Group XII invention and the species wherein R1 is acyl of 18 carbons, R2 is H, R3 is alkylene, R4 is acyl of 18 carbons, P is PEG-3400 and T is a peptide having sequence CRGDC and further the two cysteines are linked together via a disulfide linkage. Claims 3-4, 6-11, 14-35 and 61, 63-65 are directed to the elected species and thus are under consideration.

2. A search directed to the elected species was conducted. Claims 3-4, 6-11, 14-35 and 61, 63-65 are found to be free of art to the extent that they read on the elected species. Claims 66-67 are allowed

3. The search is extended to include a subgenus of claim 17 wherein R1 and R4 are acyl groups of 19-23 carbons, R2 is a lower alkyl, R3 is an alkylene, P is a PEG hydrophilic polymer and T is a targeting ligand directed to GPIIbIIIa receptor such as RGD.

Any rejection that is not addressed in this Office Action is considered obviated in view of the amendments.

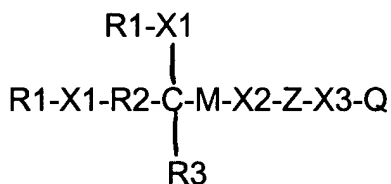
Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

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4. Claims 3, 4, 6-11, 14-17, 22-35, 61, and 63-65 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Unger et al WO 96/40285 ("WO '285").

WO '285 teaches all elements of the compounds encompassed by the instant claims; namely the subgenus described above in paragraph 4. WO'285 teaches targeted vesicles comprising a gas, lipid structures containing phosphatidylcholine, and a compound having the formula:



The compositions of WO '285 meet the limitations of the instant claims. (see pages 61-63; page 124, lines 1-21; page 135, lines 18-27; page 144, lines 14-30; page 156, lines 1-14; claim 136-149, page 179-182; claim 164, page 183).

Examiner draws Applicant's attention to WO' 285 claim 135 at page 179 lines 13-15. The compound of page 179, meets the instant diamide structure. The carbon atom of this structure is linked to $\text{R}^2\text{-X}^1\text{-R}^1$ at one end, $\text{X}^1\text{-R}^1$ at the other, and R^3 at the 3rd position. The R^2 in WO '285 is defined as an alkylene moiety of 1-30 carbons encompassing the instantly claimed ethylene. X^1 can further be -NR^4 wherein R^4 is a hydrogen or alkyl. Such moiety meets the limitation of instant N-R^5 . Finally, R^1 of the WO '285 is an alkyl of 1-50 carbons, which reads on the instant R^4 and R^2 as acyl groups having 16-23 carbons. All other limitations are described in the below table as the corresponding groups. (see claim 136-149, page 179-182; claim 164, page 183). Accordingly, when X^1 is NR^4 and R^4 is alkyl of 1-10 carbons, WO '285 teaches the

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subgenus of compounds that encompass compounds described as formula (IV) in the instant claim 17.

WO '285 also teaches that peptides such as RGD can be used as targeting agents. (see pages 50-54). In fact, the targeting agents taught by WO '285 can form cyclic disulfide bonds which meets the limitations of the instant claim 15. (see page 57, lines 23-30; page 58, line 1-page 60, line 20). WO' 285 also teaches targeted vesicles comprising liposomes comprising a phospholipid, a perfluorocarbon gas such as perfluorobutane, and a bioactive agent that can be incorporated into the targeted vesicles. The phospholipids employed by WO '284 include phosphatidylcholines such as dipalmitoylphosphatidylcholine (See page 29-30; page 90, lines 15-page 91, lines 11; page 108, lines 17-page 109, lines 32 examples 18-21, 37; claims 1-30; 170-185. Also see the table below).

The corresponding groups in the compositions of WO '285 are as follows:

Elemental groups of the Formula IV and the Instant Compositions	Rejected Species	Functional Group of the Compounds of WO '285 and the Compositional elements	Corresponding Subgenus	Citation
X1, X2	C=X3, C=X3-N(R8), -C=X3-N(R8)-C(=X3)-, wherein X3 is O or S	X2, X3	R5-X4-C(=X5)-, R5-C(=X5)-X4, -X4-C(=X5)-R5, R5-X4-C(=X5)-R5-C(=X5)-X4, wherein X1 is NR4, R3 is a H, R4 is an alkyl 1-10 carbons, R5 is a direct bond, X4 is O, NR4 or S, and X5 is O or S	Page 179, lines 15-22, 25-27. Page 180, lines 1-5
R1-N-R2 or R5-N-R4	R1=R4= acyl of 19-23, R2=R5=H or lower alkyl	X1	NR4, wherein R4 is H or lower alkyl	Page 179, lines 15. Page 180, lines 2-3
R3	Alkelene	R2	Alkelene of 1 to 30 carbons	Page 180, line 1
R1, R4	Acyl of 19-23 carbons	R1	Alkyl of 1-50 carbons	Page 179, line 27
P	Hydrophilic	Z	Hydrophilic	Page 179, line

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	polymer is a polyalkyleneoxide		polymer, such as PEG, preferably having MW of about 2000-5000	25. page 44, lines 1-6
T	Peptide directed to GPIIb/IIIa receptors	Q	Peptides directed to GPIIb/IIIa receptors such as RGD	Pages 50, 55-61, and page 179, line 26. page 183, line 13-15.
Vesicles	Gas filled Liposomes	Gas filled Liposomes	Gaseous Liposomes comprising phosphatidylcholine	Pages 83, lines 24-29, page 84, line 23-page 86, line 25; page 140, line 20-page 141, line 20; Examples page 167, lines 9-21; page 174, line 5-page 175, line 20.

WO'285 only lacks the explicit use of RGD via a PEG moiety with targeted vesicles comprising phosphatidylcholine and the claimed compound.

However, it would have been obvious to one of ordinary skill in the art at the time of invention to employ targeted vesicles of WO '285 with a PEG as a hydrophilic polymer and link the targeting agent and a diamide structure within the scope of the instant claims, because as suggested by WO'285 patent itself, PEG moieties with average MW of 2000-5000 are suitable candidates for such purpose and they can be used for attaching to RGD.

The ordinary skill in the art would have had a reasonable expectation of success in preparing formulations with parameters instantly claimed, because WO'285 explicitly describes all such parameters. Therefore, the ordinary skill in the art would have had a reasonable expectation of success to employ them for their own intended use.

Response to Arguments

5. Applicant's arguments filed July 28, 2005 have been fully considered but they are not persuasive.

Applicant argues that WO 96/40285 ("WO '285") is not a competent prior art. Applicant adds that the instant claims cannot be rejected under an obviousness grounds over a 35 USC § 102 (e) reference, if at the time of the invention claimed in the pending application, the subject matter and the claimed invention in the pending application and the reference were commonly owned. (see Response at pages 11-12). Apparently Applicant attempts to invoke the protection afforded to the common inventors of a claimed invention and a potential reference under 35 USC 103 (c).

However, Examiner states that Applicant has misapplied the rule and further can not invoke a common ownership exemption to the rejection of record, because the reference applied is under 35 USC 102 (b), not 102(e). Note that the publication date of the prior art of record. The WO '285 was published in 1996. The effective filing date of the instant case is October 30, 2000. Therefore, WO '285 qualifies as 102 (b) art.

Applicant appears to argue that 103 (c) protection may be invoked if the prior art of record qualifies under 35 USC § 102 (e). However, contrary to applicant's interpretation, such protection is only applicable when the subject matter commonly owned qualifies **only** under the subsection (e) of 35 USC section 102. see 35 USC § 103(c). Here, the WO '825 qualifies under 35 USC § 102 (b). Thus, Applicant's arguments are not persuasive, and the rejection is proper.

Allowable Subject Matter

6. Claims 66 and 67 are allowed.

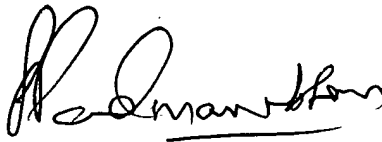
Conclusion

7. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER

PCTWORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A61K 49/00, 49/04, A61B 5/055	A1	(11) International Publication Number: WO 96/40285 (43) International Publication Date: 19 December 1996 (19.12.96)
(21) International Application Number: PCT/US96/09938 (22) International Filing Date: 6 June 1996 (06.06.96) (30) Priority Data: 08/497,684 7 June 1995 (07.06.95) US 08/640,464 1 May 1996 (01.05.96) US (60) Parent Application or Grant (63) Related by Continuation US 08/640,464 (CIP) Filed on 1 May 1996 (01.05.96) (71) Applicant (for all designated States except US): IMARx PHARMACEUTICAL CORP. [US/US]; 1635 East 18th Street, Tucson, AZ 85749 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): UNGER, Evan, C. [US/US]; 13365 East Camino La Cebadilla, Tucson, AZ 85749 (US). SHEN, Dekang [CN/US]; 2602 West Alden Street, Tucson, AZ 85745 (US). WU, Guanli [CN/US]; 2602 West Alden Street, Tucson, AZ 85745 (US).		(74) Agents: MILLER, Suzanne, E, et al.; Woodcock Washburn Kurtz Mackiewicz & Norris, 46th Floor, One Liberty Place, Philadelphia, PA 19103 (US). (81) Designated States: AU, CA, CN, JP, US, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report.</i>
(54) Title: NOVEL TARGETED COMPOSITIONS FOR DIAGNOSTIC AND THERAPEUTIC USE (57) Abstract Novel targeted compositions which may be used for diagnostic and therapeutic use. The compositions may comprise a lipid, a protein or a polymer and a gas, in combination with a targeting ligand. The targeting ligand targets tissues, cells or receptors, including myocardial cells, endothelial cells, epithelial cells, tumor cells and the glycoprotein GPIIb/IIIa receptor. The contrast media can be used in conjunction with diagnostic imaging, such as ultrasound, as well as therapeutic applications, such as therapeutic ultrasound.		